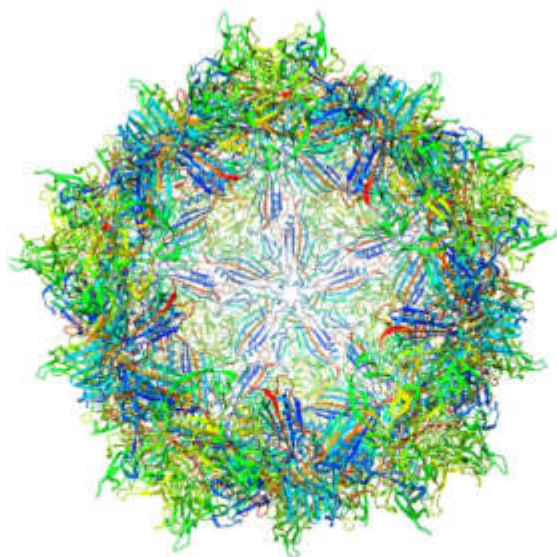


A Coronavirus Vaccine Project Takes a Page From Gene Therapy

The technique aims to make a person's cells churn out proteins that will stimulate the body to fight the coronavirus.



A rendering of the outer shell of an adeno-associated virus with the exterior partially removed. The shell is used as a Trojan horse to deliver a genetic component of the coronavirus to raise an immune response. Eric Zinn and Luk H. Vandenberghe

By [Denise Grady](#)



Researchers at two Harvard-affiliated hospitals are adapting a proven form of gene therapy to develop a [coronavirus vaccine](#), which they expect to test in people later this year, they announced on Monday.

Their work employs a method already used in [gene](#) therapy for two inherited diseases, including a form of blindness: It uses a harmless virus as a vector, or carrier, to bring DNA into the patient's cells. In this case, the DNA should instruct the cells to make a coronavirus protein that would stimulate the immune system to fight off future infections.

So far, the team has studied its vaccine candidates only in mice. Tests for safety and potency in monkeys should begin within a

month or so at another academic center, the researchers said. But two of seven promising versions are already being manufactured for studies in humans.

The research is one of at least [90 vaccine projects speeding ahead](#) around the world in desperate efforts that hold the best and probably only hope of stopping or at least slowing the pandemic. “We are presenting a different angle from everybody else,” Dr. Luk H. Vandenberghe, director of the Grousbeck Gene Therapy Center at Massachusetts Eye and Ear, said in an interview.

Their angle has several advantages, he said. One is that the type of vector, an adeno-associated virus, or AAV, is a harmless virus that is already used in two approved forms of gene therapy and has been tested in many patients and found to be safe.

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Another plus is that the technique requires very small amounts of the vector and DNA to produce immunity, so the yield of doses would be high, Dr. Vandenberghe said. Small amounts are enough because the vector is very good at getting into cells, which the DNA it carries transforms into factories that crank out the protein needed to put the immune system on alert against the coronavirus, he added.

In addition, many drug and biotech companies, large and small, already produce adeno-associated virus and could easily switch to producing the form needed for the vaccine. New facilities would not have to be built from scratch. That means production could quickly be scaled up to help meet the huge and urgent global need for vaccine.

“We are leaning on an established industry,” Dr. Vandenberghe said. “AAV as a class has had investments in the dozens of billions of dollars. There’s capacity out there that can be leveraged if we are lucky and successful.”

The approved gene therapies that use adeno-associated viruses are Luxturna, for a form of hereditary blindness, and [Zolgensma](#), for a lethal nerve disease, spinal muscular atrophy. The price of Luxturna is \$425,000 per eye. It is made and sold in the United States by Spark Therapeutics, and sold overseas by Novartis. Zolgensma, made by Novartis, is given to young children as a one-time injection, at a price of \$2.1 million.

At this early stage, Dr. Vandenberghe estimates the manufacturing cost per dose of vaccine to be from \$2.50 to \$250.

The research has the financial backing of donors, led by Wyc Grousbeck, lead owner of the Boston Celtics, his wife, Emilia Fazzalari, the chief executive of Cinco Spirits Group, and members of the Grousbeck family.

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Several other vaccine projects involve viral vectors, but no others use adeno-associated viruses.

Hundreds of AAVs infect humans and other mammals.

Researchers in gene therapy turned to them as a safer alternative after [a patient died in a study in 1999](#) from a severe immune reaction to a different type of viral vector.

For gene therapy, scientists sought adeno-associated viruses that would act as a sort of stealth carrier for DNA and not set off any inflammatory or immune response. They also tweaked the viruses genetically to prevent them from replicating inside human cells.

Working at the University of Pennsylvania about 15 years ago, Dr. Vandenberghe created a hybrid AAV from two versions found in monkeys, for possible use in gene therapy. It was no good: It provoked an immune response.

But that makes it a good candidate for a vaccine, because such a reaction can help stoke the immune system to fight the coronavirus. Many vaccines contain substances called adjuvants to help rev up the response to the vaccine itself. For this vaccine, the hybrid AAV may act not as only a vector, but also as an adjuvant.

Dr. Mason Freeman, director and founder of the translational research center at the Massachusetts General Hospital, who is planning the human tests of the vaccine, said the researchers were hoping for just enough immune response to the AAV and not too much. But the hybrid vector has never been used in humans before, so there is still much to learn.

The Coronavirus Outbreak >

Frequently Asked Questions and Advice

Updated June 5, 2020

- **Does asymptomatic transmission of Covid-19 happen?**

So far, the evidence seems to show it does. A widely cited [paper](#) published in April suggests that people are most infectious about two days before the onset of coronavirus symptoms and estimated that 44 percent of new infections were a result of transmission from people who were not yet showing symptoms. Recently, a top expert at the World Health Organization stated that transmission of the coronavirus by people who did not have symptoms was "very rare," [but she later walked back that statement](#).

- **How does blood type influence coronavirus?**

A study by European scientists is the first to document a strong statistical link between [genetic variations and Covid-19](#), the illness caused by the coronavirus. [Having Type A blood](#) was linked to a 50 percent increase in the likelihood that a patient would need to get oxygen or to go on a ventilator, according to the new study.

- **How many people have lost their jobs due to coronavirus in the**

U.S.?

The unemployment rate fell to 13.3 percent in May, the Labor Department said on June 5, an unexpected improvement in the nation's job market as hiring rebounded faster than economists expected. Economists had forecast the unemployment rate to increase to as much as 20 percent, after it hit 14.7 percent in April, which was the highest since the government began keeping official statistics after World War II. But the unemployment rate dipped instead, with employers adding 2.5 million jobs, after more than 20 million jobs were lost in April.

• Will protests set off a second viral wave of coronavirus?

Mass protests against police brutality that have brought thousands of people onto the streets in cities across America are raising the specter of new coronavirus outbreaks, prompting political leaders, physicians and public health experts to [warn that the crowds could cause a surge in cases](#). While many political leaders affirmed the right of protesters to express themselves, they urged the demonstrators to wear face masks and maintain social distancing, both to protect themselves and to prevent further community spread of the virus. Some infectious disease experts were reassured by the fact that the protests were held outdoors, saying the open air settings could mitigate the risk of transmission.

• How do we start exercising again without hurting ourselves after months of lockdown?

Exercise researchers and physicians have some blunt advice for those of us aiming to return to regular exercise now: [Start slowly and then rev up your workouts, also slowly](#). American adults tended to be about 12 percent less active after the stay-at-home mandates began in March than they were in January. But there are steps you can take to ease your way back into regular exercise safely. First, "start at no more than 50 percent of the exercise you were doing before Covid," says Dr. Monica Rho, the chief of musculoskeletal medicine at the Shirley Ryan AbilityLab in Chicago. Thread in some preparatory squats, too, she advises. "When you haven't been exercising, you lose muscle mass." Expect some muscle twinges after these preliminary, post-lockdown sessions, especially a day or two later. But sudden or increasing pain during exercise is a clarion call to stop and return home.

• My state is reopening. Is it safe to go out?

[States are reopening bit by bit](#). This means that more public spaces are available for use and more and more businesses are being allowed to open again. The federal government is largely leaving the decision up to states, and some state leaders are leaving the decision up to local authorities. Even if you aren't being told to stay at home, it's still a good idea to limit trips outside and your interaction with other people.

• What's the risk of catching coronavirus from a surface?

Touching contaminated objects and then infecting ourselves with the germs is not typically how the virus spreads. But it can happen. A number [of studies](#) of flu, rhinovirus, coronavirus and other microbes have shown that respiratory illnesses, including the new coronavirus, can spread by touching contaminated surfaces, particularly in places like day care centers, offices and [hospitals](#). But a long chain of events has to happen for the disease to spread that way. The best way to protect yourself from coronavirus — whether it's surface transmission or close human contact — is still social distancing, washing your hands, not touching your face and wearing masks.

- **What are the symptoms of coronavirus?**

Common symptoms [include fever, a dry cough, fatigue and difficulty breathing or shortness of breath](#). Some of these symptoms overlap with those of the flu, making detection difficult, but runny noses and stuffy sinuses are less common. [The C.D.C. has also](#) added chills, muscle pain, sore throat, headache and a new loss of the sense of taste or smell as symptoms to look out for. Most people fall ill five to seven days after exposure, but symptoms may appear in as few as two days or as many as 14 days.

- **How can I protect myself while flying?**

If air travel is unavoidable, [there are some steps you can take to protect yourself](#). Most important: Wash your hands often, and stop touching your face. If possible, choose a window seat. A [study from Emory University](#) found that during flu season, the safest place to sit on a plane is by a window, as people sitting in window seats had less contact with potentially sick people. Disinfect hard surfaces. When you get to your seat and your hands are clean, use disinfecting wipes to clean the hard surfaces at your seat like the head and arm rest, the seatbelt buckle, the remote, screen, seat back pocket and the tray table. If the seat is hard and nonporous or leather or pleather, you can wipe that down, too. (Using wipes on upholstered seats could lead to a wet seat and spreading of germs rather than killing them.)

- **How do I take my temperature?**

Taking one's temperature to look for signs of fever is not as easy as it sounds, as "normal" temperature numbers can vary, but generally, keep an eye out for a temperature of 100.5 degrees Fahrenheit or higher. If you don't have a thermometer (they can be pricey these days), there are [other ways to figure out if you have a fever, or are at risk of Covid-19 complications](#).

- **Should I wear a mask?**

The C.D.C. has [recommended](#) that all Americans wear cloth masks if they go out in public. This is a shift in federal guidance reflecting [new concerns that the coronavirus is being spread by infected people who have no symptoms](#). Until now, the C.D.C., like the W.H.O., has advised that ordinary people don't need to wear masks unless they are sick and coughing. Part of the reason was to preserve medical-grade masks for health care workers who desperately need them at a time when they are in continuously short supply. Masks don't replace hand washing and social distancing.

- **What should I do if I feel sick?**

[If you've been exposed to the coronavirus or think you have](#), and have a fever or symptoms like a cough or difficulty breathing, call a doctor. They should give you advice on whether you should be tested, how to get tested, and how to seek medical treatment without potentially infecting or exposing others.

- **How do I get tested?**

If you're sick and you think you've been exposed to the new coronavirus, [the C.D.C. recommends that you call your healthcare provider and explain your symptoms and fears](#). They will decide if you need to be tested. Keep in mind that there's a chance — because of a lack of testing kits or because you're asymptomatic, for instance — you won't be able to get tested.

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Like other vaccine projects, this one is focusing on the so-called spike on the coronavirus, which it uses to grab onto cells and invade them. In theory, if the immune system can be trained to make antibodies to block the spike, the virus will not be able to establish an infection.

The DNA being carried by the vector holds directions for making a protein portion of the spike. Because it is not known which section of the spike is likely to set off the best immune response, researchers test DNA for different parts.

One potential problem that every vaccine project will be on the lookout for is disease enhancement: the possibility that a vaccine, instead of preventing infection, could actually make the disease worse. Dr. Vandenberghe said his team was working with three other laboratories that would conduct tests to address this question.

Disease enhancement has become a particular concern because all the vaccine projects are trying to move so much faster than usual that there is a fear the problem could go undetected, Dr. Freeman said. It is challenging to design studies to find it, particularly with a new disease that is not well understood.

The two scientists said the many research groups forging ahead with vaccine projects were racing not against one another, but against the coronavirus.

“We need multiple shots at goal,” Dr. Vandenberghe said. “The level of unknowns of what we have to try to achieve here is too high, and the level of urgency is equally high.”

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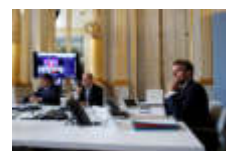
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Denise Grady has been a science reporter for The Times since 1998. She wrote “Deadly Invaders,” a book about emerging viruses. [@nytDeniseGrady](#)

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